Past and Future Applications of Adaptive Optics in Vision & Eye Care

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NEI-Biomedical Research Partnership
Outline

1. Overview of how AO systems work.
2. How AO systems are being used in basic and clinical research.
3. Future applications and challenges of AO.
Point Spread Function vs. Pupil Size

1 mm  2 mm  3 mm  4 mm  5 mm  6 mm  7 mm

Perfect Eye

Typical Eye

Courtesy A. Roorda
Aberrations in the Eye

Conventional Optics
Fix These

But Not These

Lower Order Aberrations

Higher Order Aberrations

astigmatism
defocus
astigmatism

trefoil
coma
coma
trefoil

quadrafoil
secondary astigmatism
spherical
secondary astigmatism
quadrafoil

pentafoil
secondary trefoil
secondary coma
secondary coma

Courtesy D.R. Williams
Adaptive Optics In Astronomy:

- Proposed in 1953 (Horace Babcock)
- First Implemented in mid-1970s

The laser emerging from the dome of the 120" Shane Telescope at the Lick Observatory is used for measuring atmospheric aberrations.
Adaptive optics measures and corrects the wave aberrations of the eye

- Permits large pupil (diffraction & NA)
- Increased lateral resolution
- Increased collection efficiency of reflected light
- Increased axial resolution (SLO)
Types of wavefront correctors

a) Discrete Actuator

b) Segmented: Piston only and Piston/tip/tilt

c) Membrane

d) Bimorph
OKO membrane mirror

Hamamatsu LC-SLM

Xinetics deformable mirror

AOptix bimorph
“fast, simple, & robust”

Boston Micromachines Corp.

Iris AO
Dynamic correction in one subject’s eye as revealed by measured PSF

- $\lambda = 0.78 \, \mu m$
- 6.8 mm pupil
- 30% Gain
- 21 Hz

**Before correction:**
1.6 $\mu m$ RMS

**After correction:**
0.16 $\mu m$ RMS

6 frames to converge

80 frame video
First Use of a Deformable Mirror In the Eye:

First use of wavefront sensing to correct higher order aberrations

First demonstration of retinal imaging and vision improvement by correcting higher order aberrations

First AO images on a cone dystrophy patient. Demonstrated that the mosaic was patchy due to photoreceptor dropout.

2. How AO systems are being used in basic and clinical research

High-resolution retinal imaging

- flood illumination
  - Nidek
- cSLO
- OCT
- HRT
- Stratus OCT3
- OCT3
<table>
<thead>
<tr>
<th>GROUP</th>
<th>TYPE</th>
<th>CORRECTOR</th>
<th>PERFORMANCE</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Rochester</td>
<td>Flood</td>
<td>Xinetics (37,97),</td>
<td>&lt; 0.1 μm RMS, d = 6.8 mm</td>
</tr>
<tr>
<td></td>
<td>cSLO</td>
<td>BMC (37)</td>
<td>0.12 μm RMS, d = 6 mm</td>
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<td></td>
<td></td>
<td></td>
<td>Coming Online</td>
</tr>
<tr>
<td>2. Houston</td>
<td>cSLO</td>
<td>Xinetics (37)</td>
<td>0.15 μm RMS, d = 7 mm</td>
</tr>
<tr>
<td></td>
<td>cSLO</td>
<td>BMC (144)</td>
<td></td>
</tr>
<tr>
<td>3. Indiana</td>
<td>Flood</td>
<td>Xinetics (37),</td>
<td>&lt; 0.1–0.2 μm RMS, d=6.8 mm</td>
</tr>
<tr>
<td></td>
<td>OCT</td>
<td>Xinetics (37),</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>BMC (144) &amp; AOptix (37)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>&lt; 0.1–0.2 μm RMS, d=6.8 mm</td>
</tr>
<tr>
<td>4. Murcia Murcia &amp; Vienna</td>
<td>Flood</td>
<td>OKO (37), LC-SLM (230,000),</td>
<td>0.1 μm RMS, d = 5.2 mm</td>
</tr>
<tr>
<td></td>
<td>OCT</td>
<td>OKO (37)</td>
<td>~0.1 μm RMS, d = 5.5 mm</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>~0.1 μm RMS, d = 3.68 mm</td>
</tr>
<tr>
<td>5. Imperial Col / City, UK</td>
<td>cSLO</td>
<td>OKO (37)</td>
<td>&gt; 0.35 μm RMS, d = 4 mm</td>
</tr>
<tr>
<td>6. Galway, Ireland</td>
<td>Flood</td>
<td>OKO (37)</td>
<td></td>
</tr>
<tr>
<td>7. San Diego</td>
<td>Flood</td>
<td>OKO (19)</td>
<td>~0.3 μm RMS, d = 8 mm</td>
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<td>GROUP</td>
<td>TYPE</td>
<td>CORRECTOR*</td>
<td>PERFORMANCE</td>
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</tr>
<tr>
<td>8. UC Davis / LLNL</td>
<td>Flood OCT</td>
<td>ITEK (109) BMC (144) &amp; Bimorph (37)</td>
<td>~0.1 µm RMS, d = 7 mm</td>
</tr>
<tr>
<td>9. LLNL (will be operated at Doheny)</td>
<td>Phoropter cSLO</td>
<td>BMC (144) BMC (144) and AOptix (37)</td>
<td>Online Coming Online</td>
</tr>
<tr>
<td>10. Chengdu, China</td>
<td>Flood</td>
<td>Bimorph (19 or 37)</td>
<td>&lt; 0.2 µm RMS, d = 5 mm</td>
</tr>
<tr>
<td>11. Paris</td>
<td>Flood</td>
<td>Bimorph (13)</td>
<td>&lt; 0.3 µm RMS, d = 7 mm</td>
</tr>
<tr>
<td>12. Moscow / Kestrel Corp</td>
<td>Flood</td>
<td>Bimorph (18)</td>
<td>&gt; 0.1 µm RMS, d = 4.8 mm</td>
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<tr>
<td>13. Indiana</td>
<td>cSLO</td>
<td>BMC (144)</td>
<td></td>
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2. How AO systems are being used in basic and clinical research

**High-resolution retinal imaging**

- Cone classification
- Cone-rod dystrophy
- Color vision
- Retina tracking
- Capillary blood flow
- Diabetic retinopathy
- Glaucoma (optic disc)

**Vision improvement & assessment**

Adaptive Optics for Vision Applications
Pablo Artal,
Sunday 8-8:20 am

MEMS-based Adaptive Optics Phoropter
Julianna Lin,

Adaptive Optics Phoropter
Nicholas Chateau

The Limits of High Contrast Photopic Letter Acuity With Adaptive Optics
Ethan Rossi
Turning on the AO during a 10 Hz video of the cone mosaic

- Video rate: 10 fps
- 2° FOV
- 1° ecc.
- AO correcting at 15 Hz
- 6.0 mm pupil
Cone images in one subject’s eye

No AO correction

AO correction

1° field of view; 1.25° eccentricity
Imaging cones with an AO-SLO

Courtesy S. Burns
Cone Dystrophy

Female, 30-years old

10 µm

Courtesy S. Choi & J. Werner
Cone-Rod Dystrophy (OD)

44 year-old male
VA 20/80 (corrected)

Courtesy S. Choi & J. Werner
Cone-Rod Dystrophy (OD)

Courtesy S. Choi, R. Zawadzki & J. Werner
8° TVF
7° TVF
4° TVF
2° TVF
2° NVF
10 microns

Total Deviation
Pattern

Courtesy S. Choi & J. Werner
Adaptive Optics Images of the Human Trichromatic Cone Mosaic

Courtesy A. Roorda, H Hofer, & D. Williams
Cone scintillation may be clue to cone type

Registered stack of 120 images

- High Intensity fluctuations
  - C1
- Medium fluctuations
  - C6
  - C9
- Low Intensity fluctuations
  - C11

4 sec video
30 fps
0.8° Field of view
1.4° retinal ecc.
2 msec exposure

Jungtae Rha
Adaptive optics imaging of color blind retinas

Courtesy D. R. Williams
• 28 year old Deuteranope
• No other vision problems (self-reported or clinical)
• Fundus exam within normal limits & normal acuity (20/16)

Has a normal L/M array, in that it contains L and M genes. However, the M gene encodes a pigment with a rare combination of amino acids in transmembrane segment IV:

1) Has been observed in association with BCM (pedigree H in Nathans et al., 1989), in 11 out of 11 meioses.

2) In addition, has been seen in 5 other unrelated families, in both L and M genes (Crognale et al., 2004 & Neitz & Neitz, unpublished).

3) Thus, this unusual combination is itself an inactivating mutation or is tightly linked to one.

Courtesy D. R. Williams
AO Imaging Reveals Patchy Loss of Healthy Cones

Current clinical measures are not sensitive enough to detect substantial retinal loss:

• Snellen Acuity is 20/16
• Fundus appears normal

NC, OD
1 degree Temporal

10 arcmin

Courtesy D. R. Williams
NC, Deuteranope
~3 deg FOV

(Carroll et al., 2004)
Miniature eye movements measured with an AO-SLO during fixation

- Precision: 1 arc min
- Few arc sec

SUNDAY, 8:40 – 9:00 am

Courtesy S. Stevenson
Through focus video for a fixating eye

- Video rate: ~30 fps
- 1° FOV
- 1.25° ecc.
- AO correcting at 22 Hz
- 0.1 µm RMS
- 6 mm pupil

RJ
Leukocyte Velocity Measurement

- No fluorescent dyes required (safe, long term)
- Identify ghost vessels (non-perfused capillaries)
- 95% confident of velocity changes as small as 0.076 mm/sec

Leukocyte velocity (mm/sec) in the smallest capillaries around the fovea

Blood flow in capillaries: 4-burst imaging

Capillary dia ~ 6.6 µm
Blood velocity ~ 1.5 mm/s

1.4 ° retinal ecc.
λ = 679 nm
1 msec exp
1 msec delay

w/o AO

w/ AO

50 µm
Diabetes

Courtesy A. Roorda
Imaging Glaucoma in a Monkey Model

Lamina Cribrosa

1 degree

Courtesy A. Roorda
Abhiram Vilupuru, Nalini Rangaswamy, Laura Frishman, Ron Harwerth
Volumetric imaging of retina cells with AO-OCT

High 3D resolution and sensitivity permits observation of cone cells in 3 dimensions.

SUNDAY, 12:10 – 12:20 pm
3. Future applications and challenges of AO

Technical issues
- operator friendly
- cheap & compact AO
- commercialization

Applications
- Killer application
- Depends strongly on what can be seen:
  - cone photoreceptors
  - retinal capillaries
  - ?